

FURACA #10

AIM: Preparation of FURACA from ZACA by New Route

STAGE-I: PREPARATION OF ~~TFA~~ TFA (STD).

Raw Materials:

NaSH : 37.5g

DMW : 365.0g +

2. Furoyl Chloride : 27.5g

EtoAc : (250+100) ml

NaHCO₃ : 20.0g

DMW : 175.0 ml

~~Conc HCl~~ 1:1 HCl : (48+49) ml

PROCEDURE:

1. Charge DMW, cool to $25-20^{\circ}\text{C}$.
2. Charge NaSH and stir 5' to get clear solⁿ.
3. Add Furoyl chloride in 40-45' at $20-25^{\circ}\text{C}$ and then stir 10' at same temp. +
4. Then charge EtoAc (250ml) and adjust the pH to 0.9-1.0 with 1:1 HCl at $22-25^{\circ}\text{C}$ in 15'.
5. Separate the layers. Eliminate the aq. phase.
6. To the org. phase charge DMW (175) and adjust the pH to 7.0-7.1 with NaHCO₃ at $20-22^{\circ}\text{C}$ in 15'.
7. Then stir for 30' at $20-22^{\circ}\text{C}$ and separate the layers.
8. To the rich aq. layer charge 100 ml EtoAc and again adjust the pH to 0.9-1.0 with 1:1 HCl at $20-22^{\circ}\text{C}$ in 15'.
9. Stir 15' at $20-22^{\circ}\text{C}$ and separate the layers.
10. This Org. layer (OL₂) is taken for next stage.

Vol. of OL₂ (TFA) : ~~25~~ 130.0 ml

HPLC TFA Imp.

OL₁ 97.34 (1.0+1.0)

OL₂ 97.48 2.1

STAGE-II: FURACA PREPARATION:

Mali : (A) STD. + EtOAc slurry ^{and spray} given separately.

(B) pH is adjusted to 3.0 only and the Net cake was washed with EtOAc slurry and spray.

Raw Materials:

TACA : 50.0 g
EtOAc : 200.0 g
GAA : 30.0 ml
BF₃ gas : 68.5 g.
TFA solⁿ : 130.0 ml.
EDTA : 0.3 g.

Reactions

	(A)	(B)
DMW	75.0 ml	75.0 ml
EDTA	0.15 g	0.15 g
SHS	0.5 g	0.5 g
18-20% NH ₃ sol ⁿ	48.0 ml 2.5 pH	42.0 ml 3.0 pH
DMW	(45+75+25) ml	(25+75+25) ml
EtOAc	(75+25) ml	(75+25) ml

PROCEDURE:

1. Charge EtOAc, GAA at RT and cool to 0°C.
2. Purge BF₃ gas at <10°C.
3. Add EDTA and stir 35' at 15°C.
4. Then charge TACA + stir for 5' and then charge TFA solⁿ.
5. Stir of the Rxn mixture at 30°C for 2½ hr. & monitor the Rxn. mass.
Divide the mass into two equal parts.

- Chave
- (A) ① To the one part into the pre-cooled DMW (~~75%~~ for 15°C) and add EDTA + SHS.
- ② Adjust the pH to 3.5 by 18-20% NH_3 soln. in 40-45' at 20-25-30°C
- ③ Stir for 30' at 25°C and then filter it.
- ④ Wash the product with DMW spray, slurry & spray
- ⑤ Take the wet cake in a RBF and add 75ml and stir for 15' at 25°C and then filter
- ⑥ Then give 25ml EtOH spray
- ⑦ Dry the product at 30-35°C for 2hr-3hr.
- ⑧ Quantify the washing EtOH layer.

- (B) ① Transfer the Rem. mass (another part) into the 15°C DMW and add EDTA + SHS.
- ② Adjust the pH to 3.0 by 18-20% NH_3 soln. in 40-45' at 25-30°C.
- ③ Stir for 30' at 25°C and then filter it.
- ④ Wash the product with DMW spray, slurry & spray
- ⑤ Take the wet cake into the RBF and add 75ml EtOH and stir 15' at 25°C
- ⑥ Filter it & wash with 25ml EtOH spray.
- ⑦ Dry it at 35°C for 2-3hr.
- ⑧ Quantify the washing EtOH layer.

R/M Results

Duration	TACA	FURACA	TFA	Pmp
1hr.	4.96	81.95	11.70	0.35
2hr.	0.74	89.86	7.81	0.33
2½ hr.	0.20	91.26	7.10	

Terminated in 2½ hr.

(7) OBS: (1) TFA having 2% Impurity, even though
 FURACA has gone smoothly.
 (2) Colour of the Res. mass is normal.
 (3) While adding NHz addition, the colour of
 in it (B) slurry is somewhat different, it is
 spray in greenish colour.
 (4) In both case Rate of filtration is
 7.5ml normal + material nature also
 fillz same.

	Crude Net Wt	EtoAc slurry + spray	
		Washed Wet Wt	Dry Wt
(A)	61.2 g	54.3 g	28.4 g
(B)	60.3 g	56.4 g	29.5 g

3. 80% EtOAc slurry + spray washed, ~~etc~~ EtOAc layer Wt is
 % of FURACA
 in it (A) Wt. of EtOAc only : 54.5g / 60.0ml
 spray (B) Wt. of EtOAc only : 35.4g / 40.0ml

HPLC Report

	FURACA	TACA	TFA	Imp	Cl
(A) Crude	97.37	0.35	1.17	0.31	
(B) Crude EtOAc washed	96.91	0.19	2.15	0.10	
(B) Crude EtOAc washed					

Quantitative Analysis

	FURACA	MIC	% of FURACA in EtOAc
(A) Purified	91.93	2.1	0.0033 %
(B) "	81.84	2.01	0.0022 %